DATA EVALUATION RECORD

1. **CHEMICAL:** Oxine Copper (Copper 8-Quinolinolate). Shaughnessey Number: 024002.

2. **TEST MATERIAL:** Ro 17-0099/000; Copper 8-Quinolinolate; bis-(8-quinolinolato)-copper; Batch No. 8293/3; 99.5% purity; a dark green/yellow powder.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral LD_{50} Test. Species Tested: Bobwhite quail (*Colinus virginianus*).

4. **CITATION:** Hakin, B., M.H. Rodgers and I. Grützner. 1991. Ro 17-0099/000 (Copper 8-Quinolinolate): Acute Oral Toxicity (LD_{50}) to the Bobwhite Quail. Study performed by Huntingdon Research Cenre Ltd., Huntingdon, Cambridgeshire, England, and RCC UMWELTCHEMIE AG, Itingen, Switzerland. Laboratory Study No. HLR 184-901854/RCC 284253. Submitted by La Quinoleine et ses dérivés, S.A. EPA MRID No. 429271-01.

5. **REVIEWED BY:**

Michael L. Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
Applied Sciences, Inc.

Signature: Michael L. Whitten
Date: 12-17-93 Joseph Taylor 4/5/95

6. **APPROVED BY:**

Mark A. Mossler, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature:
Date: 12-20-93

James J. Goodyear, Ph.D.
Project Officer, EEB/EFED
USEPA

Signature: Ann Stavola
Date: 4/14/95

7. **CONCLUSIONS:** This study is scientifically sound, and meets the guideline requirements for an avian oral LD_{50} test. Based on nominal concentrations, the LD_{50} was 618 mg/kg. This value classifies the test material as slightly toxic to bobwhite quail. The NOEL was not established, due to treatment-related behavioral abnormalities at all test levels.

8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:**

10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A.

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Bobwhite quail (*Colinus virginianus*) were obtained from a commercial supplier in Cambridgeshire, England, and were phenotypically indistinguishable from wild birds. The birds were acclimated to the facilities for 14 days prior to initiation of the test. The study was conducted on two separate groups of birds. The first group was approximately 4 months of age, and the second group was approximately 5 months of age.

B. **Test System:** Birds were housed indoors in pens constructed of polythene coated steel wire. Artificial lights provided 7 hours of light per day. The average minimum and maximum temperatures during the main study were 19 ± 1.2°C and 21 ± 1.2°C, respectively, with a mean relative humidity of 74 ± 7.2%. The average minimum and maximum temperatures for the later-dosed groups were 16 ± 1.3°C and 19 ± 2.2°C, respectively, with a mean relative humidity of 81 ± 9.3%.

C. **Dosage:** Single dose oral LD_{50} test. Dosages initially used were 0, 305, 488, 781, 1250, and 2000 milligrams of Ro 17-0099/000 per kilogram of body weight (mg/kg). Three groups were later dosed at 0, 119 and 191 mg/kg. The initial groups were observed for 23 days after dosing; the later groups were observed for 14 days after dosing.

D. **Design:** The birds were assigned to treatment groups based on bodyweight, with the goal of similar mean bodyweights in each group. Each group consisted of five males and five females. The birds were separated by sex into groups of 2 or 3 birds per cage. All birds were fed HRC layer diet. Food and water were supplied *ad libitum* during acclimation and during the test, except during the 18-hour period immediately prior to dosing, when food was withheld.

The six initial groups were dosed on 9/25/90. Extra groups dosed at lower levels were required due to unexpected mortality at the 305 and 488 mg/kg treatment levels. The later groups were dosed on 11/7/90.

The test substance was dispersed in corn oil. Dosages were administered by oral intubation using a syringe and

plastic catheter. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds received a corresponding volume (10 ml/kg) of corn oil. Samples of the dosing solutions were collected to verify test concentrations, and were analyzed using high performance liquid chromatography.

All birds were observed daily for mortalities, signs of toxicity, and abnormal behavior. The birds were individually weighed on days -14, -7, 0, 7, and 14. The initially dosed groups were also individually weighed on days 21 and 23. Group food consumption was determined for days -14 to -8, -7 to -1, 1 to 7, and 8 to 14 in all groups; food consumption in the initially dosed groups was also determined for days 15 to 21 and 22 to 23.

Macroscopic *post mortem* examinations were conducted on all mortalities and on ten birds from the highest surviving dosage group at study termination.

E. **Statistics:** The LD_{50} and 95% confidence interval were calculated by probit analysis.

12. **REPORTED RESULTS:** Analyses of dosing solutions showed that measured concentrations of test material were within the range of 93.4 to 115.9% of nominal values.

There were no mortalities in the initial or the later-dosed control group. All birds in the control groups were normal in appearance and behavior throughout the study.

There was 10%, 50%, 50%, 90% and 100% mortality at the 305, 488, 781, 1250, and 2000 mg/kg test levels, respectively (Table 1, attached).

Behavioral signs of toxicity consisted of a subdued appearance, unsteadiness, ruffled feathers, liquid excreta, and prostrate posture. One or more of these signs were noted in all treatment groups, with the severity and time to recovery varying directly with increasing dosage.

Group bodyweights and food consumption were decreased in all groups dosed at or above 305 mg/kg during days 0-7 (Tables 2 and 3, attached).

Most abnormalities noted at necropsy consisted of colored and/or enlarged crops and gastrointestinal tracts. In many cases, the gastrointestinal tract contained a greenish brown fluid.

DP Barcode : D195529
PC Code No : 024002
EEB In : 10/05/93
EEB Out :

To: Kathryn Davis
Product Manager 52
Special Review and Reregistration Division (7508W)

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch/EFED (7507C)

Attached, please find the EEB review of...

Reg./File # : 024002-042567
Chemical Name : Oxine-copper (copper 8-quinolinolate)
Type Product :
Product Name :
Company Name : La Quinoleine S.A.
Purpose : Review avian acute and dietary studies

Action Code : 627 Date Due : 05/01/95
Reviewer : J. Sylvester

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT
71-1(A)	42927101 42927102	Y	72-2(A)			72-7(A)		
71-1(B)			72-2(B)			72-7(B)		
71-2(A)	42927103		72-3(A)			122-1(A)		
71-2(B)	42927104		72-3(B)			122-1(B)		
71-3			72-3(C)			122-2		
71-4(A)			72-3(D)			123-1(A)		
71-4(B)			72-3(E)			123-1(B)		
71-5(A)			72-3(F)			123-2		
71-5(B)			72-4(A)			124-1		
72-1(A)			72-4(B)			124-2		
72-1(B)			72-5			141-1		
72-1(C)			72-6			141-2		
72-1(D)						141-5		

Y=Acceptable (Study satisfied Guideline)/Concur
P=Partial (Study partially fulfilled Guideline but additional information is needed
Supplemental (Study provided useful information but Guideline was satisfied)

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The oral LD_{50} was 618 mg/kg, with a 95% confidence interval of 478 to 803 mg/kg. A slight treatment related effect (abnormal behavioral observations) was noted at 119 mg/kg, the lowest treatment level tested.

The report contained statements certifying that the study was inspected by the laboratory's Quality Assurance department. The GLP statement was as follows: "The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 40 CFR Part 160."

14. **REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:**

A. **Test Procedure:** The test procedures were in accordance with Subdivision E and SEP guidelines with the following exceptions:

The birds were not randomly assigned to groups. Instead, the assignments were based on bodyweight, with the goal of similar mean bodyweights in each group.

All groups were not tested concurrently. The two lowest treatment groups were dosed 43 days after the initially dosed groups.

B. **Statistical Analysis:** The reviewer used EPA's Toxanal computer program to calculate the LD_{50} value (attached printout). The LD_{50} (618 mg/kg) and confidence interval were the same as reported by the authors. The slope of the dose response curve was 4.1.

C. **Discussion/Results:** Two additional treatment groups and one control group were dosed 43 days after the initial groups were dosed. Normally, this would be unacceptable for a toxicity test. In this case, however, no birds died in the later dosed groups. The LD_{50}, therefore, is not affected by the addition or deletion of the later groups.

The birds were not randomly assigned to groups. Instead, the assignments were based on bodyweight, with the goal of similar mean bodyweights in each group. This method of assignment probably did not affect the outcome of the test. The registrant, however, should enact procedures in future tests that provide random assignments to groups.

Based on nominal concentrations, the LD_{50} was 618 mg/kg, classifying the test material as slightly toxic to bobwhite quail. The NOEL was not established, due to treatment-related behavioral abnormalities at all test levels. The study is scientifically sound, and meets the guideline requirements for an avian oral LD_{50} test.

D. **Adequacy of the Study:**

(1) **Classification:** Core.

(2) **Rationale:** N/A.

(3) **Repairability:** N/A.

15. **COMPLETION OF ONE-LINER:** Yes; December 10, 1993.

DER MRID # 429211-01 OXINE COPPER

Page _____ is not included in this copy.

Pages 7 through 9 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

M.L. WHITTEN OXINE COPPER Colinus virginianus 12-10-93

****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
2000	10	10	100	9.765625E-02
1250	10	9	90	1.074219
781	10	5	50	62.30469
488	10	5	50	62.30469
305	10	1	10	1.074219
191	10	0	0	9.765625E-02
119	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 305 AND 1250 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 617.3558

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
6	.1144041	617.6233	474.3323	854.5744

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	.1573833	1	.7376048

SLOPE = 4.11254

95 PERCENT CONFIDENCE LIMITS = 2.481031 AND 5.744049

LC50 = 618.3001

95 PERCENT CONFIDENCE LIMITS = 478.4362 AND 803.1363

LC10 = 303.66

95 PERCENT CONFIDENCE LIMITS = 175.4738 AND 404.9661

****

Ecological Effects Branch One-Liner Data Entry Form

Chemical Oxine Copper Shaughnessy No. 024002 Pesticide Use Fungicide

AVIAN ORAL TOX SPECIES (AGE)	% AI	LD_{50} (95%CL)	SLOPE	NOEL	STUDY/REVIEW DATES	MRID/ CATEGORY	LAB	RC
1. Colinus virginianus 4-5 months	99.5	618 mg/kg (478-803)	4.1	not established	1991/1993	429271-01 CORE	HRC	MCW
2.								
3.								
4.								
5.								

AVIAN DIETARY SPECIES (AGE)	% AI	LC_{50} (95%CL)	SLOPE	NOEL	STUDY/REVIEW DATES	MRID/ CATEGORY	LAB	RC
1.								
2.								
3.								
4.								
5.								

COMMENTS: _____